Applicants thank Examiner Sisson for pointing out in paragraphs 8 and 9 of the office action that the proprietary nature of trademarks should be respected. Applicants have amended the specification as suggested by the examiner.

In paragraphs 10-12 of the office action, Examiner Sisson rejected claims 23-50 under 35 U.S.C. §112. In paragraph 10, Examiner Sisson stated that claims 23-50 contain subject matter that was "...not described in the specification in such a way as to enable one skilled in the art...to make and/or use the invention." See the paragraph bridging pages 3 and 4 of the office action. The examiner summarizes the §112 rejection by stating in paragraph 12 of the office action that "...the specification has not been found to enable the claimed method and as such, claims 23-50 are rejected under 35 U.S.C. §112, first paragraph." See page 8 of the office action. Accordingly, the §112 rejection appears to be based solely on the examiner's allegation of lack of enablement.

Two specific issues were raised in the office action. The first issue was raised in the paragraph bridging pages 4 and 5. There, the examiner states:

> The specification does not disclose just what constitutes BioDadoo nor how such a compound is made. Normally, the commercial availability of a compound would not lead to a need for greater enablement. However, in the present case, Boehringer-Mannheim Biochemicals no longer exits (merged with Roche) and the product is not commercially available.

Accordingly, the examiner expressed his opinion that the specification does not satisfy the enablement requirement of §112.

First, it is not accurate to state that the specification does not disclose what constitutes BioDadoo. Dadoo is identified at page 5, line 7, 1,8-diamino-3,6-

In addition, the introduction to example 5 starting at page 17, line 11 makes clear that the purpose of the example is to label DNA probes with biotin.

Nor is it accurate to say that BioDadoo is no longer commercially available. While the Examiner is correct in stating that Boehringer-Mannihem has merged with Roche, Boehringer-Mannihem was not the sole source of BioDadoo. BioDadoo is also available from Pierce. The product description from Pierce is enclosed for the examiner's review. BioDadoo is product no. 21346, and is called EZ-Link™ Biotin-PEO-Amine.

The second enablement issue was raised in paragraph 11 of the office action. There, the examiner expresses his opinion that the specification does not disclose a generic method by which the entire family of compounds useful in the claimed method can be prepared without undue experimentation.

Applicants strenuously, but respectfully, disagree. This issue was extensively discussed in applicants' amendment dated January 4, 2001 at pages 14-18. The office action dated March 22, 2001 refers to the January 4, 2001 amendment, but does not state why the arguments made therein are not persuasive.

The examiner is respectfully requested to review pages 14-18 of the January 4, 2001 amendment at this time. Applicants are confident that upon doing so, Examiner Sisson will agree that the full scope of claims 23-50 are fully enabled in compliance with §112.

Briefly, the reactions involved in making the compounds useful in the invention are all well known and easily conducted under standard conditions by a person having ordinary skill in the art. Enablement is especially apparent, since, as

noted by the examiner on page 6 of his office action, the skill in the art is "...high, on par with those that hold a Ph.D. in biochemistry."

The application provides extensive examples of how representative compounds according to the invention can be prepared. These examples include starting materials (example 1) and final products (examples 2A, 2B and 2C). Example 3A provides a method for preparing dGTP, a purine nucleotide. Example 3B provides a method for preparing 5-AA-dUTP, a pyrimidine nucleotide. Examples 4 and 5 provided methods for labeling DNA molecules.

The reactions involved in preparing the compounds useful in the method of claims 23-50 as well as for labeling a nucleotide with such compounds involve standard chemistry that would require no undue experimentation for the person having ordinary skill in this art who, to emphasize, has been identified by the examiner as being highly skilled.

Applicants respectfully request the examiner to explain more precisely what he believes has not been enabled, and to explain why he does not believe Applicants' arguments in their amendment dated January 4, 2001 pages 14-18 are inadequate to overcome these rejections.

This application is now believed to be in condition for allowance. Notice to that effect that the examiner's earliest convenience is respectfully requested.

The Commissioner is hereby authorized to charge any fees or additional fees associated with the communication or credit any over-payment to Deposit Account No. 08-2461. A duplicate copy of this sheet is attached.

Respectfully submitted,

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VERSION OF AMENDMENT WITH MARKINGS TO SHOW CHANGES MADE

IN THE SPECIFICATION:

Replace the paragraph starting at page 18, line 27 with the following paragraph:

Direct spot blot

HPV-6 probe (batch # 061094) labeled with biotin according to the invention was 10-fold serially diluted into spot buffer comprising 900mM sodium chloride, 90mM sodium citrate and 200 µg/ml single stranded salmon sperm DNA giving a dilution series varying from 1000-0.1 pg biotin probe per µl. 1 µl spots were applied onto nitrocellulose membrane and incubated for 2 hours at 80°C to blind the DNA. The biotin probe was visualized using a streptavidin-alkaline phosphatase conjugate (Sigma) combined with a NBT/BCIP precipitating substrate solution (Sigma) according to the following protocol:

-Membranes were soaked in TBS solution containing 0.5% ~~tween 20~~ TWEEN20 (TBST) for 5 minutes.

-Membranes were incubated with Strep-AP (3 DEA U/ml) in TBST for 15 minutes at 37°C.

-NC-membranes were washed 3 times 5 minutes in TBS solution followed by a 5 minute wash step in demineralised water.

-Membranes were incubated with NBT/BCIP substrate solution for 15 minutes at 37°C, subsequently washed in demineralised water and air dried.